UNIVERSITY OF PENNSYLVANIA

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F. WILLIAM SUNDERMAN

A THESIS

IN MEDICAL SCIENCES

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PARTIAL FULFILLMENT OF THE REQUIREMENTS FOR
THE DEGREE OF DOCTOR OF PHILOSOPHY

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STUDIES OF SERUM ELECTROLYTES

IV. THE CHLORIDE AND NITROGEN BALANCES, AND WEIGHT CHANGES IN PNEUMONIA[1]

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In an earlier study (1) data were presented on the changes in the blood serum during the course of lobar penumonia. It was found that the concentration of total base, chloride, and protein in the serum was usually decreased during the active infection. Following the crisis these concentrations returned to their normal values, the chloride less rapidly than the total base. The low excretion of chloride in the urine during the precritical period has long been known and the inference has been drawn that there is a correlation between the urinary excretion and the serum concentration. No satisfactory explanation of the mechanism of the change in composition of the serum or of the decreased urinary excretion of chloride has been established, but from studies in the literature it has often been inferred that during the precritical period the body tissues retain chloride which is subsequently released during the epicritical period. In an attempt to obtain data on factors concerned in these changes, studies of the intake and output were undertaken in patients suffering with lobar pneumonia.

To review completely the very extensive literature upon the chloride concentration of the serum and urine in pneumonia seems unnecessary since this has been done by many authors, notably by Hutchison (6), Von Moraczewski (8),

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Garratt (7), and Peabody (9). The conclusion of the earlier workers that chloride was retained in the body during the febrile period arose chiefly from the observation that the addition of chloride to the diet during this period was not accompanied by a corresponding increase of chloride excretion. These observations were later supplemented by analyses of tissues and studies of chloride balance. Von Moraczewski (8) reported 18 cases of pneumonia in which daily amounts of chloride, nitrogen, phosphorus, and calcium in the food, urine, and feces were determined. Only three times in his series, twice when the food intake was very small and once when calcium phosphate was administered, did he find the daily excretion of chloride in the urine and feces in excess of the daily intake of chloride. He observed that although the excretion of chloride in pneumonia parallels in general the intake of chloride, nevertheless, an excessive ingestion of salt was not accompanied by the normally prompt excretion.

Hutchison (6) reported 4 cases that excreted less chloride in the urine during the febrile period than was taken with the food, but these patients received from 1.0 to 7.5 grams of chloride per day. Hutchison found no evidence from tissue analyses that chloride tended to accumulate in any particular organ during pneumonia, but rather that all of the organs seemed to contain somewhat more chloride per unit of weight than normally.

In order to determine how much chloride could be retained in the pneumonic exudate, Peabody (9) analyzed the lungs in two cases of pneumonia in which one lung was normal and the other hepatized. He found that a retention of about two grams of sodium chloride could be credited to the pneumonic lung. The skin of pneumonia patients showed no significant increase in its salt content. Von Hösslin (10) averaged the percentile concentration of chloride in normal and pneumonic lungs from his own data and from data of Jarish (11), Meillère (12), Hutchison (6), and Terray (13) and found that the mean sodium chloride concentration in pneumonic lungs in 14 observations was 0.343 per cent of fresh weight and in 10 estimations in normal lungs, 0.331 per cent. Taking the weight of a normal lung at 250 grams and a hepatized lung at 1250 grams, there would be an increase of about 3.5 grams of sodium chloride in the latter.

Sandelowsky (2) gave from 3 to 36 grams of sodium chloride in 3 days to patients convalescing from pneumonia. He used himself as a control and observed in the pneumonia patients a greater delay in the excretion of the sodium chloride.

Prigge (14) upon injecting from 100 to 150 cc. of a 25 per cent solution of sodium chloride intravenously into patients during the precritical period of lobar pneumonia also observed a lagging in the excretion of the chloride, although the blood concentration fell the day following injection and thus behaved as in normal individuals.

Holten (15) fed pneumonia patients during the precritical period a diet which contained between 6 and 7 grams of sodium chloride daily and found that less than the corresponding amount of chloride was excreted in the urine until about the time of crisis.

Leyden (5) in 1869 was perhaps the first to study weight changes in pneumonia. He observed in his patients an increased loss of weight through the skin and lungs during the febrile period and a rapid loss following the crisis. Sandelowsky (2) studied the body weights in 11 cases of pneumonia. In 7 cases the body weight either increased slightly during the precritical period or remained constant, whereas, after the crisis the weight fell more or less rapidly; in 4 there was a continued decrease in weight during the febrile and afebrile periods.

Garnier and Sabareanu (3) observed that pneumonia patients do not always lose weight in the early stages of the disease but that even with a small food intake, they sometimes gain weight. The gain in weight in their cases did not generally exceed 500 grams per day but was in one instance as high as 2000 grams in three days. With fall in temperature the weight dropped. In children suffering with pneumonia the gain in weight before the crisis would appear to occur more frequently than in adults. Lussky and Friedstein (4) observed in their series of children that the weight remained constant or was increased before crisis, but was decreased with the disappearance of fever. Only one out of their 28 cases occurring in children failed to show loss of weight following the crisis.

MATERIAL AND METHODS

These studies were carried out on seven patients with lobar pneumonia. In five patients study was commenced between the fifth and eighth days of the disease. Two patients, selected because they were admitted on the third day of the disease, were treated with large doses of sodium chloride by mouth. The period of investigation for each patient was from 2 to 11 days and except in one fatal case extended 1 to 8 days following the crisis. The patients selected were young adult males who had all been healthy before the onset of pneumonia. In addition two normal individuals were followed by similar methods of study for 48 hours on a diet comparable with that received by the patients. The normal individuals were subjected each day to a cabinet light bath designed to promote a loss of water through the skin which would approach in magnitude that occurring in the patients.

On admission the patients were placed in a special metabolic room and were under constant observation during the period of study, one patient or occasionally two being studied at a time. Each morning at 7 o'clock the patient was weighed. A silk scale of the type proposed by Benedict and Root (16), which weighs accurately to 10 grams, was used and was fitted with an especially constructed thin stretcher. With the exception of the first 2 days of study in Case B3, no patient received any food for at least 8 hours before weighing time, and none received water or food between 5:30 and 7 o'clock in the morning. The patient was encouraged to defecate and void during the half hour before weighing. If unable to void, he was catheterized.

The daily intake consisted of weighed amounts of the following ingredients: milk, grape juice, tea, canned tomato and pea purees, triscuit, sugar, salt and water. The diet corresponded to the type given to the hospital patients suffering

from lobar pneumonia but was designed to contain articles which have an approximately uniform chemical analysis. Analyses of the commercial foods were furnished to us by the respective manufacturers; these were supplemented by our own analyses and by values taken from the Food Bulletin of the Connecticut Agricultural Experiment Station (17). The chloride content of the foods was analyzed.

In one patient (B3) a high caloric diet consisting of cream, milk, eggs, and malted milk was given for 2 days.

Enemas that were given contained small amounts of soap.

The collected measured output included urine, feces, sputum, and blood removed for analysis. These were weighed to a gram. Toluol was used to preserve the urine. The excreta were kept refrigerated. An attempt to collect the sweat was unsatisfactory.

The dry weights of excreta and the nitrogen contents of the urine and feces were determined. The total amount of nitrogen excreted per day in the sputum was found in two analyses to be negligibly small. The chlorides were analyzed according to Van Slyke's method (18) in serum and food and Volhard's in urine. The Kjehldahl method was used for nitrogen determination.

RESULTS

In table 1 are given data on the food intake, nitrogen and chloride balance and changes of weight. The day of crisis is designated as the zero day and days before and after as − and + respectively. An estimate of the caloric requirement has been made from normal basal standards for weight and age with an addition for fever, estimated by the average percentile increase of metabolism per degree increase of temperature from Du Bois' data (19) and an added 10 per cent during the precritical period. The caloric value of the diets was consistently low and the nitrogen balance markedly negative. An attempt to increase the intake of food in patient B3 led to serious tympanites and for this series of studies such attempts were not repeated. Patients B6 and B7, who were given large doses of sodium chloride, took more food spontaneously during the precritical period without deleterious symptoms.

Weight changes

Loss of weight was usually present in both precritical and postcritical periods as would be expected with such an inadequate diet. In table 2 is shown the relative daily loss of weight in grams per kilogram of initial weight and the negative nitrogen balance per kilogram

of initial weight for the patients studied and, for comparison, similar data from a series of fasting experiments from Benedict's (20) collection of studies. The weight curve during the postcritical period of B5 was possibly modified by the development of a pleural effusion. B6 and B7 received large amounts of NaCl which in B7 were poorly excreted and led eventually to slight visible edema. Patients B3 and B4 exhibited increased loss of weight following the crisis associated with unchanged or with less negative nitrogen balance and less caloric deficit. A similar increased loss of weight following the crisis was noted by Leyden (5) and interpreted by him to indicate precritical storage of water and postcritical release. The behavior of the weight curves resembles that observed in fasting studies. The fluctuations in the rate of loss of weight from day to day can be approximately duplicated in fasting studies. Partial inanition is evidently an important factor in inducing the observed changes in weight with apparently additional factors diminishing the rate of loss of weight before the crisis, and increasing it after the crisis.

That nitrogen equilibrium is not maintained in pneumonia has been demonstrated by many workers, including von Moraczewski (8), Cook (21), and Leyden and Klemperer (22). The negative nitrogen balance in the pneumonia patients was higher than in fasting subjects doubtless because of the greater metabolism in the former. The loss of weight per milligram of negative nitrogen balance was less in the precritical periods in all the patients and throughout the study of B5 and in the two subjects receiving salt than in the fasting subjects. This might be considered indirect evidence of relative retention of water during the precritical period. In the postcritical periods of B3 and B4 the loss of weight was closely comparable with that observed in the fasting subjects.

Excretion through skin and lungs

In table 1 are given the data on the urinary loss of water and the loss of weight through skin and lungs. The loss of water through skin and lungs is equal to the total loss of weight through skin and lungs minus the difference between weight of CO_2 given off and of O_2 absorbed through the lungs. This difference of weight is about 75 $\pm$75 grams per day. It is evident from these data that from 25

TABLE 1

Data on cases

Case number	Day from crisis	Temperature*	Initial weight and daily change	Urinary water	Weight loss skin and lungs	Intake				Estimated caloric deficit	Nitrogen output	Nitrogen balance	Chloride intake	Chloride output					Chloride balance	Expected chloride balance ±50 per cent	Relative chloride balance	Amount of sputum
						Protein	Carbohydrate	Fat	Calories					Urine	Feces	Sputum	In blood removed for analysis	Total				
		°F.	gm.	gm.	gm.	gm.	gm.	gm.			gm.	gm.	mM.	mM.	mM.	mM.	mM.	mM.	mM.	mM.		gm.
B1			50,466																			
	−1	103	− 359	1,002	3,040	25	77	38	755	1,400	17	−13	17	0.2	2.5	5.1	3.0	20 ±9	−3 ± 9	−13	?	88
	0	104	− 396	1,024	2,744	26	102	31	799	1,300	20	−16	17	0.0		11.6	4.6	25 ±9	−8 ± 9	−14	?	152
	+1	98	− 1,412	999	2,714	30	87	35	786	800	22	−17	21	0.7	1.3	5.8		17 ±9	+4 ± 9	−49	+	86
B2			48,138																			
	−3	105	+ 148	1,342	2,196	38	112	46	1,067	1,300	23	−17	36	36.9		2.8	4.2	53 ±9	−17 ±10	+5	−	35
	−2	105																				
B3			86,138																			
	−3	104	+ 186	1,473	2,436	86	215	153	2,733	900	26	−12	137	18.7		8.1	4.0	40 ±9	+97 ±12	+7	+	108
	−2	104	− 640	1,494	2,174	46	118	74	1,412	2,200	27	−20	89	10.8	2.4	3.7	5.3	31 ±9	+58 ±11	−22	+	57
	−1	103	− 1,260	1,616	2,197	0	8	0	33	3,200	26	−26	0	4.1		3.8		17 ±9	−17 ± 9	−44	?	50
	0	105	− 1,106	1,327	4,276	12	52	14	391	3,100	23	−21	7	2.9		2.8		15 ±9	−8 ± 9	−39	+	43
	+1	100	− 610	1,813	2,584	41	141	47	1,160	1,600	36	−29	27	3.3	0.3	1.6	3.8	18 ±9	+9 ±10	−21	+	12
	+2	100	− 623	2,067	2,080	52	110	63	1,227	1,600	27	−19	39	11.4		2.6		23 ±9	+16 ±10	−22	+	31
	+3	100	− 1,324	2,964	2,382	48	100	57	1,117	1,700	31	−23	111	57.3	1.7	1.8	3.8	74 ±9	+37 ±11	−46	+	20
	+4	98	− 1,141	2,715	2,274	64	143	74	1,500	800	26	−16	98	76.3	1.4	3.4		90 ±9	+7 ±11	−40	+	40
	+5	98	− 554	2,306	1,829	33	132	36	1,002	1,300	23	−18	125	155.0		0.5		165 ±9	−40 ±12	−19	?	6
	+6	98	− 1,559	2,259	1,997	35	148	35	1,060	1,200	20	−14	74	164.0	1.5		3.3	178 ±9	−104 ±10	−54	−	0
	+7	98	− 639	1,919	1,690	11	100	9	555	1,700	17	−15	86	134.0				143 ±9	−58 ±11	−22	−	0

B4			60,934																				
	−2	104	+ 149	1,419	3,223	30	87	37	800	1,900	32	−27	22	39.5			5.0	54 ±9	−32 ± 9	+5	−	0
	−1	103	+ 149	1,716	3,223	35	104	42	939	1,700	32	−26	25	31.6	0.6	1.8	1.8	45 ±9	−20 ±10	+5	−	60
	0	102	− 2,020	2,983	3,086	34	90	40	861	1,600	32	−27	25	37.6		1.0	3.6	51 ±9	−26 ±10	−71	+	26
	+1	99	− 1,950	1,667	2,554	28	93	34	798	1,400	26	−22	20	21.0	3.6		2.8	36 ±9	−17 ± 9	−68	+	0
	+2	99	− 1,013	1,443	1,909	27	75	33	698	1,500	22	−18	20	17.7				27 ±9	−7 ± 9	−35	+	8
	+3	99	+ 156	1,716	1,689	34	107	41	936	1,300	24	−19	24	16.7	1.9	0.3	1.9	30 ±9	−6 ± 9	+5	?	7
	+4	98	− 1,086	3,031	1,631	35	124	41	1,014	800	17	−11	24	29.0				38 ±9	−14 ± 9	−38	?	3
	+5	98	− 582	2,178	1,499	33	122	35	943	900	18	−13	56	21.7			3.3	34 ±9	+22 ±10	−20	+	5
	+6	98	+ 283	1,569	2,029	49	212	48	1,508	300	17	−14	143	48.9		0.7		59 ±9	+84 ±12	+10	+	11
	+7	98	+ 276	3,360	717	100	188	172	2,707		21	−5	152	164.0	0.9		2.2	176 ±9	−24 ±12	+10	−	0
	+8	98	− 794	2,147	927	67	155	113	1,924		23	−13	121	171.0	2.1			182 ±9	−61 ±11	−28	−	0
B5			26,528																				
	−3	103	− 198	1,520	1,774	35	92	42	890	600	13	−7	26	22.9	2.1	0.1	2.0	36 ±9	−11 ±10	−7	?	24
	−2	104	− 284	2,405	924	30	83	36	773	800	14	−9	22	30.2	0.4	2.9		43 ±9	−21 ± 9	−10	?	36
	−1	103	− 56	1,679	813	27	94	32	782	700	11	−7	19	13.6		4.6	3.1	30 ±9	−11 ± 9	−2	?	47
	0	103	− 731	2,340	896	27	108	32	840	700	14	−10	19	13.2	3.0	3.8		29 ±9	−11 ± 9	−26	?	45
	+1	100	− 389	1,922	941	24	92	26	707	400	9	−5	43	4.1	0.9	2.4	3.3	20 ±9	+23 ±10	−14	+	28
	+2	100	+ 730	1,601	649	46	187	45	1,361		8	−1	94	4.9		1.4		15 ±9	+78 ±11	+26	+	19
	+3	100	+ 398	961	825	56	111	98	1,557		11	−2	132	9.4	3.4	0.1		22 ±9	+110 ±12	+14	+	10
B6			50,625																				
	−5	102	− 468	1,788	2,516	40	116	48	1,063	900	18	−12	137	17.3		4.6	3.5	34 ±9	+103 ±12	−16	+	48
	−4	101	+ 751	1,420	2,085	53	130	64	1,303	500	21	−16	211	37.0	1.5	14.2		62 ±9	+149 ±13	+26	+	97
	−3	101	+ 78	2,140	1,970	55	137	63	1,340	500	15	−6	296	112.0	0.6	10.4	5.5	138 ±9	+158 ±15	+3	+	86
	−2	101	− 545	1,909	1,822	46	158	58	1,369	400	16	−13	291	231.0	1.3	9.5	4.2	255 ±9	+36 ±15	−19	+	64
	−1	101	− 64	1,941	1,856	49	148	59	1,340	500	14	−6	527	346.0	1.0	14.2		370 ±9	+157 ±20	−2	+	119
	0	101	− 674	2,342	1,758	45	157	51	1,299	500	12	−5	344	316.0		6.3	4.3	336 ±9	+8 ±16	−24	+	60
	+1	100	− 333	1,915	1,815	50	138	57	1,270	400	13	−5	332	288.0	0.3	6.5		304 ±9	+28 ±16	−12	+	54
	+2	100	− 609	1,746	2,064	51	152	60	1,370	300	13	−5	315	292.0	0.3	6.5	4.3	312 ±9	+3 ±15	−21	?	49
	+3	100	− 879	1,577	1,822	48	127	51	1,187	500	14	−6	224	295.0	0.6	7.7		312 ±9	−88 ±13	−31	−	52
	+4	100	− 752	1,196	1,878	45	105	53	1,090	600	12	−5	351	192.0	0.2	3.4		205 ±9	+146 ±16	−26	+	24

TABLE 1—*Concluded*

Case number	Day from crisis	Temperature*	Initial weight and daily change	Urinary water	Weight loss skin and lungs	Intake				Estimated caloric deficit	Nitrogen output	Nitrogen balance	Chloride intake	Chloride output					Chloride balance	Expected chloride balance ±50 per cent	Relative chloride balance	Amount of sputum
						Protein	Carbohydrate	Fat	Calories					Urine	Feces	Sputum	In blood removed for analysis	Total				
		°F.	gm.	gm.	gm.	gm.	gm.	gm.			gm.	gm.	mM.	mM.	mM.	mM.	mM.	mM.	mM.	mM.		gm.
B7			59,278																			
	−6	104	0	1,107	1,703	39	113	46	1,030	1,400	10	−4	96	2.0		15.1	3.8	30 ±9	+66 ±11	0	+	149
	−5	102	+ 7	1,090	2,113	44	97	53	1,050	1,100	12	−5	203	2.9	6.3	11.2		29 ±9	+174 ±13	0	+	90
	−4	100	+ 914	2,115	1,278	52	108	63	1,207	900	25	−17	296	24.8		10.9	4.1	49 ±9	+247 ±15	+32	+	80
	−3	100	+ 129	1,932	1,658	46	109	57	1,137	1,000	19	−12	291	71.5	6.9	12.7	4.1	104 ±9	+187 ±15	+5	+	113
	−2	100	+ 1,211	1,952	795	42	122	51	1,137	1,000	12	−5	530	116.6		13.1		139 ±9	+391 ±20	+42	+	100
	−1	100	+ 1,602	1,293	989	42	122	51	1,137	1,000	18	−11	344	83.4	1.8	13.8	4.5	113 ±9	+232 ±16	+56	+	106
	0	99	+ 1,715	983	872	47	103	57	1,117	900	10	−2	239	47.0	1.4	9.4		67 ±9	+172 ±14	+60	+	72
	+1	99	+ 340	1,004	1,018	29	87	35	790	1,200	9	−4	41	38.4	0.9	12.5	4.4	65 ±9	−24 ±10	+12	−	83
	+2	98	− 354	1,022	802	20	71	23	595	1,300	8	−5	34	39.5	0.9	10.2		60 ±9	−26 ±10	−12	?	78
	+3	98	− 71	1,097	868	36	92	43	910	1,000	9	−3	69	40.9	0.5	10.6		61 ±9	+8 ±10	−2	?	76
Normal subjects																						
B8			68,046																			
	1		− 865	1,336	2,502	37	81	40	830	1,500	13	−10	34									
	2		− 482	1,059	2,092	39	85	41	850	1,400	13	−7	34									
B9			74,184																			
	1		− 1,411	2,703	2,079	36	70	38	765	1,700	11	−5	17									
	2		− 843	1,676	2,034	36	75	40	800	1,700	13	−7	34									

* Average of maximum and minimum temperatures for the day.

TABLE 2

Weight and nitrogen balance in pneumonia and in fasting subjects (from literature)

Subject	Period, days	Loss of weight, grams per kilogram per day			Negative N balance, mgm. per kilogram per day			Weight loss / N balance	Caloric deficit / Caloric need
		Mean for period	Maximum	Minimum	Mean for period	Maximum	Minimum		
Fasting men									
Succi	3rd to 12th	9.2	20.6	1.6	169	242	118	55	1.00
	3rd to 12th	7.9	15.9	1.6	151	214	110	52	1.00
	3rd to 12th	7.2	10.3	+1.6					1.00
	3rd to 12th	7.9	17.5	+1.6	114	154	80	69	1.00
	3rd to 12th	8.1	14.3	+4.8					1.00
	3rd to 12th	8.4	24.6	0					1.00
	3rd to 12th				129	155	88		1.00
	3rd to 12th	6.2	9.7	4.2					1.00
Jacques	3rd to 12th	7.3	30.2	+3.2					1.00
Beanté	3rd to 12th	6.7	12.3	0	157	208	127	43	1.00
Schenk	3rd to 12th	5.5	12.5	1.8	114	141	78	48	1.00
L	3rd to 12th	7.1	12.5	1.8	172	195	161	41	1.00
Pneumonia									
B3	Precritical	6.7			225			30	0.61
	Postcritical	10.8			226			48	0.62
	Total	9.8	18.1	+2.2	226	338	140	43	0.62
B4	Precritical	(+) 2.4			435			(+) 6	0.68
	Postcritical	12.3			259			47	0.37
	Total	9.6	33.2	+4.6	291	443	82	33	0.44
B5 (pleural effusion)	Precritical	0.7			290			2	0.46
	Postcritical	0.0			170			0	0.08
	Total	0.3	2.8	+2.8	221	377	38	1	0.27
B6 (with salt)	Precritical	0.1			209			0	0.30
	Postcritical	1.2			103			12	0.27
	Total	0.7	1.7	+1.5	156	316	99	4	0.29
B7 (with salt)	Precritical	(+) 10.9			152			(+) 72	0.49
	Postcritical	(+) 6.9			59			(+) 117	0.56
	Total	(+) 9.3	6.0	+29.0	115	286	34	(+) 81	0.52

per cent to as high as 80 per cent of the total water output in these subjects is by way of the skin and lungs. This is correlated of course with the visible sweating observed through much of the period studied. Such visible sweating precludes the possibility of calculating metabolism by the method of Benedict from the loss of weight through skin and lungs. Marked increase in loss of weight by skin and lungs just at the time of the crisis was not an outstanding feature of our cases. The high skin-lung loss of weight in the normal subjects, B8 and B9, was the result of a daily cabinet bath.

It is noteworthy that although the normal subjects B8 and B9 forced drinking of water to the point of discomfort they did not attain the level of water intake and water output reached by the pneumonia patients without any especial persuasion.

Chloride balance

Our chloride balance studies may be divided into two groups consisting of four patients (B1, B2, B4 and B5) who received no unusual form of treatment; and three patients (B3, B6 and B7) two of whom were given excessive quantities of salt (B6 and B7) and the other (B3) who was given a relatively high caloric diet during the first two days of observation. The chloride in the daily intake of food, water, and enema was measured as well as the chloride output through the urine, feces, sputum, and blood removed for analysis. An allowance of ± 2 per cent has been made for maximum error.

The attempt was made to collect sweat for chloride analysis. Strips of lint which had been washed free from chloride with distilled water were tied on to the patient's forehead, axillae, and nape of the neck. At frequent intervals the entire body was dried with other strips. However, it proved impossible to obtain satisfactory collections by this method. The best data relative to sweat in pneumonia that was found was that of Schwenkenbecker and Spitta (23). These investigators placed patients on a rubber cloth washed free from chloride and covered them with chloride free linen. After 24 hours they washed the individual and coverings first with water, then with alcohol, and determined the chloride content of the fluid collected. Their conclusion that not more than 1 gram of sodium chloride was excreted daily in the sweat in diseases with profuse sweating such as

pneumonia is consistent with the present observations, for although the collections of sweat in this study were unquestionably incomplete, the maximum daily recovery which was obtained in 19 attempts was 0.27 gram NaCl. To allow for the chloride in the sweat 0.5 gram NaCl, with an allowance for error of ±0.5 gram, was arbitrarily added to the measured daily output of chloride.

In table 1 are presented the individual daily chloride balances. The total daily output includes the allowance for sweat. The balance is designated as positive when the intake exceeds the output.

The first group of our cases (B1, B2, B4 and B5) showed daily chloride loss during the precritical period. Even assuming that no chloride was excreted in the sweat, the chloride balance was negative during 8 out of 10 critical and precritical days in these patients. In B3, B6, and B7, on the other hand, there was a daily retention of chloride 15 out of 17 critical and precritical days. The 2 days in which the balance was negative in this group occurred in B3 on the −1 and 0 day at a time when very little food was taken. Case B3 had been given a relatively high caloric diet on the −3 and −2 days of his disease which had to be discontinued on the days following on account of tympanites. After the crisis in the first group and in B3 there was retention of chloride during the first 4 days. During the same period B7 showed a definite loss of chloride and B6, fluctuations in the balance.

This evidence suggests that more chloride is excreted than ingested during the precritical period in lobar pneumonia when the patients receive no forced diet or excessive quantity of salt and that the situation is reversed when larger quantities of chloride are given.

A question which arises in considering the chloride balance is its relation to gain or loss of body water. Associated with a gain or loss of body weight we may properly expect a positive or negative chloride balance respectively. Taking 35 mM. per kilogram of body weight as the mean concentration of chloride in the body as a whole, we may approximate an expected chloride balance from a given change in weight. This has been done subject to an allowance of 50 per cent for error and the increase or decrease of chloride so estimated from the change in weight has been designated in the table as the *expected chloride balance*.

The difference between the chloride balance and the expected chloride balance has been indicated merely in a directional manner in the table as the *daily relative chloride balance.* The direction of this quantity has been indicated by + and − signs where the difference has exceeded the sum of the allowances for error. It must be understood that this *relative chloride balance* is an approximation with respect to increase or decrease in the mean chloride concentration in the body as a whole.

B2 and B4 appear to have had definitely a relative chloride loss during the precritical period; B3, B6, and B7, a relative chloride gain; and within the large allowance for error, B1 and B5 had neither clear gain nor loss. During the first 4 days following the crisis a relative gain in chloride was apparent in B1, B3, B4, and B5. In B6 and B7 the diminished chloride intake after the crisis makes it useless to attempt interpretation of that period.

It would appear, therefore, that in the pneumonia patients who received a small intake of chloride per day the mean concentration of chloride in the water of the body either remained unchanged or decreased during the precritical period; whereas after the crisis it increased. In those patients who received a larger intake of chloride there was a gain in the mean concentration of chloride in the body before the crisis and either a gain or loss after the crisis.

Clinical observations on four lobar pneumonia patients receiving excessive amounts of sodium chloride

Because of the decreased excretion of chloride in the urine sodium chloride has been given by many therapeutically, often by hypodermoclysis. Haden (24) suggested that sodium chloride should be administered orally to all patients with lobar pneumonia to keep the blood chlorides near the normal level. He gave 74 grams of salt in 4 days to one patient in addition to that taken with food. During these 4 days only 7.23 grams were excreted in the urine. The concentration of chloride in the blood was between 62 and 67 mM. per liter followed by a subsequent rise to 82 mM., whether related or not to the crisis is not stated. Later Haden (25) reported the clinical course and the blood and urinary chloride analyses in three cases of lobar pneumonia receiving excessive quantities of salt. Except in one case the excessive salt intake was not clearly associated with a rise in the blood chloride.

TABLE 3

Serum changes in cases on ordinary diet and in cases receiving extra salt

Case number	Type of organism	Day of disease from crisis	Total base		Serum chloride	Serum protein		Serum specific gravity
			Chemically determined	1.17 × serum corrected conductivity		Serum total nitrogen × 6.25	Serum protein (refractometric)	
			m.Eq. per liter	*m.Eq. per liter*	*m.Eq. per liter*	*grams per liter*	*grams per liter*	*20°C./20°C.*
B1	Pneumococcus Type IV	−1	136	140	85	79	74	1.0232
		0	140	144	85	70	76	1.0285
		+2	144	146	85	72	76	
B2	Pneumococcus Type III	−3	149	144	92	70	65	
B3	Pneumococcus Type IV	−3	148	145	87	75	76	
		−2	149	149	91	75	80	
		+1	146	153	89	78	88	
		+3	143	151	94	73	74	
		+6			99	78	81	
		+8	157	156	97	77	78	
B4	Pneumococcus Type II	−2	166	154	99	67	53	
		−1	158	146	88	65	62	
		0	158	142	84	65	60	
		+1		146	86	65	62	
		+3	149	153	93	71	86	
		+5	148	146	95	75	78	
		+7		153	96	76	80	
		+9	148	150	95	76	81	
B5	Pneumococcus Type I	−3		146	91	70	70	
		−1	146	142	87	67	68	
		+1	138	146	86	71	80	
B6*	Pneumococcus Type IV	−5	137	151	83	63	62	1.0235
		−3	143	150	89	65	60	1.0234
		−2	146	150	95	59	56	1.0234
		0	140	149	99	64	59	1.0240
		+2	149	151	95	66	65	1.0239
		+5	149	150	91	72	71	1.0247

* Cases receiving salt therapy.

TABLE 3—*Concluded*

Case number	Type of organism	Day of disease from crisis	Total base		Serum chloride	Serum protein		Serum specific gravity
			Chemically determined	1.17 × serum corrected conductivity		Serum total nitrogen × 6.25	Serum protein (refractometric)	
			m.Eq. per liter	*m.Eq. per liter*	*m.Eq. per liter*	*grams per liter*	*grams per liter*	*20°C./20°C.*
B7*	Pneumococcus Type III	−6	142	155	90	74	72	1.0255
		−4	143	151	93	80	63	1.0246
		−3	143	152	99	66	60	1.0231
		−1	161	159	108	64	59	1.0235
		+1	155	159	104	64	59	1.0240
		+4	153	152	98	69	62	1.0226
B10*	Pneumococcus Type IV	−5	142	146	93	76	76	1.0281
		−4	155	153	100	71	73	1.0266
		−1	163	169	99	75	84	1.0290
		+1	148	151	101	65	65	1.0230
B11*		−4			91			
		−1			91			
		+1			101			

In a previously reported series of cases (26) no outstanding change was found in the serum chloride concentration or clinical course in patients receiving doses of sodium chloride with the food. A statistical analysis of the serum chloride concentrations in those patients showed no significant deviations from the values observed in patients not receiving extra salt. However, in the present study, where considerably more salt was given, increase in the serum chloride concentration is suggested in three cases. In the patients not receiving salt the concentration of serum chloride decreased until the time of crisis in 6 out of 8 patients (cases reported in 1926 (1) and present cases not receiving salt therapy); whereas, in 3 of the 4 cases receiving large quantities of salt the serum chloride concentration progressively increased until the crisis after which salt administration having been stopped, it fell. This is shown in table 3. With the administration of these larger amounts of salt certain clinical effects have been observed which will be described.

In the present group of four patients, each patient received in divided

doses from 15 to 30 grams of sodium chloride per day in the form of a 13.5 per cent sodium chloride solution. The patients objected surprisingly little to these large doses.

Abdominal distention

All four of the patients appeared to have less abdominal distention after salt was given. The abdomen became soft and required less use of stupes or other measures designed to relieve distention. The patients took a slightly higher caloric diet than those not receiving salt, perhaps because of the diminished tympanites. In view of the increased metabolism in pneumonia, it may be accepted that a higher caloric diet than is ordinarily given would be desirable provided the patients could tolerate it. A higher caloric diet without extra salt was tried in B3 but had to be abandoned on account of the abdominal distention which developed.

Sputum excretion

In 14 precritical observations in pneumonia on patients who were receiving no chloride therapy the average amount of sputum collected was 55 grams per day containing 3.7 mM. of chloride per day. In 13 precritical observations in patients receiving large quantities of salt, the excretion of sputum averaged 91 grams per day and contained 11.2 mM. of chloride per day. In the patients not given salt the chloride concentration in the sputum was 67 mM. per kilogram, whereas under larger salt intake it became 124 mM. per kilogram, a higher concentration than was present in the serum. The fact that the concentration was higher than in serum may simply be the result of evaporation of water in the respiratory tract.

These facts suggest that the retention of chloride observed during the precritical period when large amounts of salt were given, may in part be explained by the increase of chloride in the pneumonic exudate

Temperature

The temperature curve in the patients studied appeared to descend in a general way to a lower level when large doses of salt were given. Whether this was incidental can only be decided on the basis of a large series. The temperature instead of varying between 101° and

104° became less fluctuating in type and varied between 99° and 101°. No other drugs than sodium chloride and occasionally codeine sulphate were given to three of the patients; the other, B10, received chloral, barbital, and sodium bromide on several occasions. In cases B6 and B7 the temperature did not remain continually within the normal range until after the first week following what we considered to be the crisis.

Complications

In three of the four patients postcritical pleural collections and unresolved pneumonic areas were suspected from physical signs and x-ray studies. The patients presented elevations of temperature and moderate leucocytosis after the crisis. The signs were never sufficiently definite to necessitate aspiration and the abnormal chest findings disappeared in the course of about a week. As a result, however, convalescence was protracted by approximately a week.

In studies now in progress there has been substituted for large doses of NaCl a salt mixture containing per diem: KCl, 6 grams; $NaHCO_3$, 5.9 grams; $MgCl_2$, 1.2 grams. One-half of this mixture when added to the ordinary food intake of the patient provides a mean normal salt ration. The caloric value of the diet has also been increased by 500 to 1000 calories with beverages containing 10 per cent glucose.

I wish to express my gratitude to Professor J. Harold Austin for his advice throughout these studies.

SUMMARY

The total daily ingesta and egesta have been measured before and after the crisis in a series of seven patients suffering with lobar pneumonia. The body weight, nitrogen and chloride balances were determined daily. The loss of weight and inadequacy of the diet have been described and discussed. Partial inanition was an important factor in inducing the observed loss of weight, although additional factors appeared to diminish the rate of loss of weight before the crisis and to increase it after the crisis. The negative nitrogen balance in the pneumonia patients was higher than in fasting individuals.

Patients receiving the usual low caloric diet without extra salt exhibited before the crisis a negative chloride balance, the excretion exceeding the intake. This was true in spite of the extremely reduced excretion in the urine. After the crisis when more food was being taken, chloride excretion in the urine increased, but, nevertheless, there was usually a positive chloride balance. Patients who received a larger intake of chloride during the precritical period either from a more liberal diet or from large doses of salt had precritical retention of chloride.

The chloride balance has been considered also in relation to the change in body weight. In patients receiving a small intake of chloride, the mean concentration of chloride in the body appeared to be decreased before the crisis and increased after the crisis; whereas, in patients receiving a larger intake of chloride (5 to 30 grams NaCl daily) the mean concentration of chloride in the body appeared to be increased before the crisis and decreased after the crisis when the chloride administration had been stopped.

The present studies of the chloride balance do not support the view that pneumonia is characterized by a retention of chloride during the precritical period, but rather that it is characterized during the precritical period by a diminished capacity of the body to conserve chloride on a low intake of chloride and a diminished capacity to excrete chloride on a high intake of chloride. After the crisis the chloride balance becomes restored to normal from whichever deviation had earlier developed.

The clinical picture observed in four patients who received large doses of sodium chloride precritically has been described.

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PROTOCOLS

Case B1 (*Number 962*). Italian, male, age 34, butcher. The patient was admitted to the hospital with a consolidation of the left lower lobe. Crisis occurred on the 9th day of the disease. The sputum yielded a Type IV pneumococcus. The leucocyte count was 37,000 with 83 per cent polymorphonuclears on admission. Convalescence was uneventful.

Case B2 (*Number 1358*). White, male, age 21, clerk. The patient was admitted to the hospital on the 6th day of the disease with a consolidation of left lower lobe. He was cyanotic and breathing rapidly. On the 2nd day of hospitalization he became irrational, developed hiccoughs, and died. The blood and sputum both yielded a Type III pneumococcus. The leucocyte count on admission was 3,000 but became elevated to 16,000 prior to death.

Case B3 (*Number 1208*). Colored, male, age 40, laborer. Study of this patient was commenced on the 5th day of a left lower lobar pneumonia. Crisis occurred on the 8th day. During the first 2 days of observation, the patient was given a more liberal diet than usual which had to be discontinued on account of the marked abdominal distention. The patient perspired profusely on the day of the crisis. The sputum yielded a Type IV pneumococcus. The leucocyte count increased progressively from 20,000 on admission to 32,000 at the time of crisis and then fell.

Case B4 (*Number 1046*). Colored, male, age 35, laborer. The patient was first studied on the 6th day of his disease at which time he was very ill and had a consolidation of both lower lobes. Respirations were voluntarily restricted due to pleural pain. Over the left chest pleural and pleuro-pericardial frictions were audible. Abdominal distention was marked. The sputum yielded a Type II pneumococcus. Crisis occurred on the 8th day of the disease. The leucocyte count was 34,000 2 days after the crisis. Convalescence was uneventful.

Case B5 (*Number 1086*). Colored, male, age 11, school boy. Study was begun on the 7th day of the disease when the patient had consolidation of the entire left lung. The sputum yielded a Type I pneumococcus. Crisis occurred on the 10th day of the disease and was followed by the development of an interlobar empyema. A thoracotomy was performed and pus drained. The pus contained Type I pneumococcus. The highest leucocyte count was 50,000 and was observed at the time of crisis. Convalescence lasted 6 weeks.

B6 (*Number 1510*). White, male, age 47, longshoreman. The patient was first studied on the 3rd day of a left lobar pneumonia. The sputum yielded a Type IV pneumococcus. Crisis occurred on the 9th day of the disease. The temperature, however, did not maintain a postcritical normal level but continued to be elevated (99–101°) during the first week after the crisis. Physical signs, x-ray studies, and a leucocytosis of 28,000 at this time suggested the possibility of a pleural collection or unresolved pneumonic areas. These chest findings gradually disappeared without treatment. Convalescence was protracted.

This patient had been given large doses of sodium chloride during the precritical period.

Case B7 (*Number 1491*). Colored male, age 57, laborer. The patient was first studied on the 3rd day of a left lower lobar pneumonia. He was breathing rapidly and appeared toxic. Sputum contained a Type III pneumococcus. A crisis was not definitely observed but was suggested on the 10th day of the disease. Physical signs, x-ray evidence, and a leucocytosis of 15,000 later suggested the possibility of an unresolved pneumonia or pleural collection. These signs, however, disappeared. Temperature reached the normal level one week after the time that was regarded as the crisis. The urine contained on 2 occasions traces of albumin and hyaline and granular casts. Following the intake of large doses of sodium chloride during the epicritical period, the patient showed some puffiness especially of the face and a slight edema of the legs.